

The Correlation of Interphase Chromatin Structure with the Radiation-induced Inter- and intrachromosome Exchange Hotspots

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To investigate the relationship between chromosome aberrations induced by radiation and chromatin folding, we reconstructed three dimensional structure of chromosome 3 and measured the physical distances between different regions of the chromosome. Previously, we have investigated the location of breaks involved in inter- and intrachromosomal type exchange events in human chromosome 3, using the multicolor banding *in situ* hybridization (mBAND) technique. In human epithelial cells exposed to both low- and high-LET radiations *in vitro*, we reported that intra-chromosome exchanges occurred preferentially between a break in the 3p21 and one in the 3q11 regions, and the breaks involving in inter-chromosome exchanges occurred in two regions towards the telomeres of the chromosome. Exchanges were also observed between a break in 3p21 and one in 3q26, but few exchanges were observed between breaks in 3q11 and 3q26, even though the two regions are located on the same arm of the chromosome. In this study, human epithelial cells were fixed at G1 phase and the interphase cells were hybridized using the XCyte3 mBAND kit from MetaSystems. The z-section images of chromosome 3 were captured with a Leica and an LSM 510 Meta laser scanning confocal microscopes. A total of 100 chromosomes were analyzed. The reconstruction of three dimensional structure of interphase chromosome 3 with six different colored regions was achieved using the Imaris software. The relative distance between different regions was measured as well. We further analyzed fragile sites on the chromosome that have been identified in various types of cancers. The data showed that, in majority of the cells, the regions containing 3p21 and 3q11 are colocalized in the center of the chromosome, whereas, the regions towards the telomeres of the chromosome are either physically wrapping outside the chromosome center or with arms sticking out. Our results demonstrated that the distribution of breaks involved in radiation-induced inter and intra-chromosome aberrations depends upon both the location of fragile sites and the folding of chromatins.